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10/554,252	01/18/2007	William C Sessa	YU/110	2742

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ROPES & GRAY LLP
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EXAMINER	
MERTZ, PREMA MARIA	

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1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,252	SESSA ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-45 and 49-54* is/are pending in the application.

4a) Of the above claim(s) *39-41,44,45 and 49-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/30/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 14 (claims 42-43) in the reply filed on 8/4/08 is acknowledged. The traversal is on the grounds that the restriction is improper since the inventions of Groups 13-16 and 18-23 are directed to overlapping subject matter. Applicants contend that searches of the inventions of Groups 13-16 and 18-23 are co-extensive because each of these groups relate to vascular remodeling, and involves the use of Nogo-B or an active fragment thereof. Applicants argue that Group 13 is directed to promoting angiogenesis, which is a form of vascular remodeling, Groups 14 and 15 are directed to treating and preventing pathological vascular remodeling, respectively, Group 16 is directed to promoting vascular quiescence, Group 18 is directed to reducing neointima formation, Group 19 is directed to inhibiting vascular injury-induced vascular narrowing or occlusion, Group 20 is directed to preventing vascular injury-induced ischemia through vascular remodeling, Group 21 is directed to promoting endothelial cell adhesion, spreading and migration, Group 22 is directed to inhibiting vascular smooth muscle cell migration, and Group 23 is directed to treating vascular injury. However, contrary to Applicants arguments, the different Groups are drawn to different methods of treatment of different patient populations and therefore Applicants arguments are moot with respect to the searches for the different Groups being co-extensive even though NogoB is administered in each of the methods.

The test for propriety of a restriction is not whether the inventions are related but rather whether they are distinct and whether it would impose a burden on the examiner to search and

examine multiple inventions in a single invention. The inventions are distinct because a search of the literature for a method of, for example, promoting angiogenesis, would not necessarily be expected to reveal art for a method of preventing vascular injury-induced ischemia, which searches are extensive requiring separate searches and treatment of different patient populations which would be unduly burdensome.

Having shown that these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different and recognized divergent subject matter as defined by MPEP § 808.02, the Examiner has *prima facie* shown a serious burden of search (see MPEP § 803). Therefore, an initial requirement of restriction for examination purposes as indicated is proper.

The Groups as delineated in the restriction requirement 4/4/08 are patentably distinct one from the other such that each invention could, by itself, in principle, support its own separate patent (as shown by the arguments put forth in the written restriction requirement).

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112, first paragraph, scope of enablement

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2a. Claims 42-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating in ischemia in a subject in need thereof by

administering an effective amount of a composition comprising a fragment comprising amino acids 1-200 of the N-terminus of Nogo-B, does not reasonably provide enablement for a method as recited in claim 42. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn very broadly to methods of treating all types of vascular remodeling ranging from asthma to myocardial infarction. However, other than the treatment of ischemia (see specification, Example 11, pages 59-61), the specification fails to provide any guidance for the successful treatment of all these other methods.

The specification delimits the instant method to administering an N-terminal fragment of Nogo-B consisting of amino acids 1-200 out of the 373 amino acid isoform of Nogo which is Nogo-B. (see page 14, lines 16-27; page 26, lines 22-25). However, with respect to claims 42-43, as recited, what is claimed in the instant invention broadly encompasses a method of administering "all" fragments of Nogo-B that have biological activity. The specification is non-enabling for a method of administering these unlimited and unidentified fragments, which are encompassed by the scope of the claims. Claim 1, for example, is a single means claim (M.P.E.P. 2164.08(a)). In In re Hyatt, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), the Courts have held that: A single means claim, i.e. where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph. (A single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification disclosed at most only those means known to the inventor). Since no material limitations for

"fragment of Nogo-B" have been recited in the claim and only "a biological activity" has been recited, the claim encompasses every conceivable structure (means) for achieving the stated property (result), a fact situation comparable to Hyatt. The claimed invention encompasses a method of administering fragments of Nogo-B not envisioned or described in the specification, and neither does the specification disclose how these compositions can be distinguished from each other. The specification only enables a method of treating ischemia administering an N-terminal fragment of Nogo-B consisting of amino acids 1-200 out of the 373 amino acid Nogo-B, this polypeptide having specific characteristics and properties. These properties may differ structurally, chemically and physically from other known proteins. By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) quantity of experimentation, (2) guidance presented, (3) the predictability of the art, and (4) the breadth of the claims, in the instant application, the quantity of experimentation to determine which other substances are encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little, thereby rendering the results of the methods taught in the specification unpredictable (see pages 59-61). Therefore, it would require undue experimentation to determine which fragments of Nogo-B having "a biological activity" would be encompassed by the scope of the method claims. The disclosure of these a single fragment of Nogo-B is clearly insufficient support under the first paragraph of 35 U.S.C. 112 for claims, which encompass a method of administering every and all fragments, including analogs of such. In In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), the Courts have held that:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Furthermore, the amount of embodiments corresponding to the desirable compositions, may be innumerable, and the enabled embodiments amount to only one. Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe administering any other polypeptides other than an N-terminal fragment of Nogo-B consisting of amino acids 1-200 out of the 373 amino acid of Nogo-B, and since it is deemed to constitute undue experimentation to determine all the others, the disclosure is not commensurate with the scope of the claims. It is suggested that by employing

conventional claim language, the method claims be amended to include the specific polypeptide supported by the instant specification.

Furthermore, the claims as recited encompass a method of treating every and all pathologic vascular remodeling states known to man, including diabetes and coronary artery disease.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Given the inherent unpredictability of physiological activity, which would include biological processes, i.e., methods of treatment, a certain amount of enablement beyond mere assertion must be required.

The CAFC decision (Genentech Inc. v. Novo Nordisk, 42 USPQ2d 1001, 1997) expressly states that:

"When there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

If Applicants will kindly review page 1404 of In re Wands, they will find that the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

In the instant case, the method of treating coronary artery disease, is very different from a method of treating vascular disease associated with diabetes. Furthermore, the limited results presented for treatment of ischemia (inadequate blood supply (circulation) to a local area due to blockage of the blood vessels to the area), are not sufficient to enable the breadth of the claims and are not predictive of in vivo efficacy for treatment of all pathological vascular remodeling states. The treatment of pathological vascular remodeling has been the subject of intense study for the past several decades. Many promising treatments and therapies have been identified via in vitro experiments, and have not lived up to expectations when tested in vivo. In fact, the number of such treatments, which have failed to live up to their promise exceeds those, which

have been performed as hoped by orders of magnitude. The disclosure fails to teach one of ordinary skill in the art a method of treatment of all types of pathological vascular remodeling. The effectivity of the claimed method against one type of condition characterized by pathological vascular remodeling might be different from another specific type of pathological vascular remodeling depending on the developmental stage of the condition.

Thus, it would require undue experimentation on the part of the skilled artisan to use the claimed method for treated as recited, in the absence of sufficient information to predict the results with an adequate degree of certainty. In view of this unpredictability in the treatment of different pathological vascular remodeling, there cannot be said to be any reasonable expectation of success at the in vivo application of a potential therapy for all types of pathological vascular remodeling, especially in view of the fact that the current specification as filed presents only working examples pertaining to the method of treatment of ischemia in vivo. Therefore, a method for treating all types of pathological vascular remodeling as recited in claim 42 has not been enabled by the specification. Given the breadth of claim 42 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of skill in the art to practice the claimed invention.

Claim rejections-35 U.S.C. 112, second paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 42-43, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 42 is rejected as vague and indefinite for several reasons.

Claim 42, line 1, is improper because it recites the non-elected condition “preventing”.

Claim 42, is vague and indefinite because it fails to recite the specific condition to be treated.

Claim 42, line 3, recites the limitation "fragment" which can encompass a single amino acid. The metes and bounds of the term “fragment” are unclear.

Claim 42, line 4, is vague and indefinite because it recites “a biological activity”. The metes and bounds of this term are unclear because it is unclear which ‘biological activity” of Nogo-B is intended to be claimed.

Claim 43 is rejected as vague and indefinite insofar as it depends on the above rejected claim 42 for its limitations.

Conclusion

No claim is allowed.

Claims 42-43, are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Prema Mertz/
Primary Examiner
Art Unit 1646